Multifocal Conduction Blocks in Sarcoid Peripheral Neuropathy

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Abstract

Peripheral neuropathy is a rare manifestation of sarcoidosis, and previous studies have shown axonal degeneration as the main pathology. We herein report three patients with sarcoidosis who presented with multiple mononeuropathy as the initial manifestation. Nerve conduction studies showed prominent multifocal conduction blocks in the intermediate nerve trunk. In all three patients, corticosteroid treatment resulted in a dramatic clinical improvement associated with rapid resolution of conduction blocks. The sequential electrodiagnostic findings suggest that demyelinating or ischemic-functional conduction block is responsible for their neuropathy. To date, only three cases of acute conduction block neuropathy associated with sarcoidosis have been reported, but it may occur more frequently than expected.

Key words: sarcoidosis, sarcoid neuropathy, conduction block, demyelination, ischemia

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Introduction

Neurosarcoidosis is a rare manifestation of sarcoidosis, and occurs in approximately 5% of sarcoid cases (1-5). Previous reports have demonstrated the wide range of clinical phenotypes of sarcoid neuropathy. Symmetric axonal sensorimotor polyneuropathy is the most common type (2, 6, 7), but the spectrum of sarcoid neuropathy includes chronic symmetrical sensory polyneuropathy, multifocal motor neuropathy, Guillain-Barre-like syndrome (2, 7), mononeuropathy multiplex, polyradiculopathy (6), small-fiber neuropathy (1, 4), multiple painful sensory mononeuropathies (9), and lumbosacral plexopathy (7). We report three consecutive patients with subacute sarcoid mononeuropathy multiplex caused by multifocal conduction blocks in the intermediate nerve segments.

Case Report

Patient 1

A 69-year-old woman developed subacute asymmetric weakness and paresthesias in her lower limbs. Three months previously, she noticed a tingling sensation in her left foot, and 4 weeks later, in the right foot and glaucoma associated with uveitis. She became unable to walk because of bilateral leg weakness. On examination, she had asymmetric weakness in her lower extremities; on the MRC scale, muscle strength of the tibialis anterior and triceps surae was graded 4/5 on the right, and 3/5 on the left. In the upper extremities, only the right ulnar nerve was involved; muscle strength of the abductor digiti minimi, and dorsal interosseous was graded as 3/5. There was a moderate decrease in touch and vibratory sensation in the distal four limbs. Achilles tendon reflexes were absent.

Trans-bronchial lung biopsy showed non-caseating granu-
lomas consistent with sarcoidosis. She was treated with intravenous methylprednisolone 1,000 mg daily for 3 days, followed by oral prednisolone 60 mg every other day. One week after the initiation of treatment, her symptoms were dramatically improved, and she was able to walk three weeks after medication.

**Patient 2**

One year before admission to our hospital, a 57-year-old woman had blurred vision in her right eye, and was diagnosed as suffering uveitis. Six months later, she noticed weakness and paresthesias in her right leg, and 3 weeks later, muscle weakness in her left leg. On examination, muscle strength of the tibialis anterior and triceps surae was graded 4/5 on the right, and 3/5 on the left with mild impairment of pain sensation in the legs especially on the left. Deep tendon reflexes were absent in the lower extremities and diminished in the upper extremities. Multiple subcutaneous nodules were found in the back of her right hand, and their biopsy showed non-caseating granulomas. She was treated with oral prednisolone 30 mg daily, resulting in substantial improvement in muscle weakness 4 weeks after the start of therapy.

**Patient 3**

Nine months before admission, a 65-year-old woman had photophobia, and was diagnosed as having uveitis. Four weeks later, she experienced paresthesia and muscle weakness in her left hand and both legs. She could not walk without assistance because of drop feet. On examination, muscle strength was graded as 4/5 in the left triceps, 3/5 in the left wrist extensors and flexors, 2/5 in the tibialis anterior and triceps surae bilaterally. Deep tendon reflexes were absent. Sensory examination showed hyperalgesia in her feet.

Trans-bronchial lung biopsy of a mediastinal lymph node showed non-caseating granulomas. She was treated with intravenous methylprednisolone, 1,000 mg daily for 3 days, which was followed by oral prednisolone 60 mg every other day. Muscle weakness lessened day by day, and she was able to walk without assistance two weeks after the initiation of corticosteroid therapy.

**Neurophysiologic Examination**

Nerve conduction studies were sequentially performed using the conventional procedures with a standard electromyography machine (Viking 4, Nicolet Biomedical Japan, Tokyo, Japan). Motor nerve conduction studies were made on the bilateral median, ulnar, peroneal and tibial nerves. Amplitude of compound muscle action potentials (CMAPs) was measured.

Table 1 summarizes the results of motor nerve conduction studies for these three patients. In patient 1, the initial studies demonstrated conduction block in the forearm segments of the right ulnar nerve (Fig. 1A), and leg segment of the tibial and peroneal nerves. The abnormal amplitude reduction gradually resolved over the next 5 months. Patient 2 showed prominent conduction block in the leg segment of the right tibial nerves that was normalized 5 months later. In patient 3, the first examination showed conduction block in the forearm segment of the right ulnar nerve, and leg segment of the right tibial nerve (Fig. 1B). The follow-up studies revealed the reversal of conduction block.

**Discussion**

The present cases were characterized by subacute mononeuropathy multiplex and multifocal conduction blocks in the intermediate nerve trunk. The diagnosis of sarcoidosis was made at the time of neurological examination by biopsy of the swollen lymph nodes or subcutaneous nodules. Non-neurological clinical manifestation was uveitis alone. After treatment with corticosteroids, all three patients showed rapid improvement in neuropathy associated with resolution of multiple conduction blocks.
So far, conduction block in sarcoid neuropathy has been reported only in three patients (2, 10). In the first case, nerve biopsy showed necrotizing vasculitis, and abnormal CMAP amplitude reduction was replaced by reduced distal CMAP amplitudes, suggestive of axonal loss (8). The serial change suggests Wallerian degeneration. After focal infarctive axonal injury due to vasculitis, the distal stump could survive for several days or possibly weeks. At this stage, distal stimulation could elicit normal CMAP. However, distally-evoked CMAPs gradually decreased in serial studies strongly suggest Wallerian degeneration as the main pathophysiological mechanism. By contrast, the second and third patients had preserved distal CMAPs throughout the course of the disease (10). Because nerve biopsy showed that sarcoid granulomas in the endoneurium caused compression and distortion of nerve fibers, the authors propose the possibility of compression-induced demyelination. The serial electrophysiologic findings were similar to those in our three patients.

We think that either demyelinating or ischemic conduction block could be responsible for neuropathy in our patients. This argument has been often made on the pathophysiology of entrapment neuropathy. A number of morphological and physiological factors can cause nerve conduction block, apart from demyelination. These include axonal depolarization and sodium channel blockade (11). Nerve ischemia appears to be important in nerve compression. Ischemia paralyzes the electrogenic sodium-potassium pump, and thereby causes membrane depolarization (12). Depolarization block may explain the time-course of conduction block seen in the present patients. The precise pathophysiology of sarcoidosis is unknown at present, but corticosteroids could suppress the inflammatory or edematous reaction associated with non-caseating granulomas by sarcoidosis, and thereby compression ischemia in our patients.

Whatever the mechanisms, conduction blocks may represent an early stage of sarcoid neuropathy, and early treatment can lead to a favorable outcome, as shown in our patients. We suggest that sarcoid neuropathy should be considered as the cause of multifocal conduction block, and it may occur more frequently than expected.

References


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